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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,465	12/09/2003	Jeffrey A. Whitsett	10872/0507287	5274

26874 7590 08/21/2008

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EXAMINER	
MONTANARI, DAVID A	
ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
08/21/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@fbtlaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/731,465	WHITSETT ET AL.	
	Examiner	Art Unit	
	DAVID MONTANARI	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/5/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) *1-38,41 and 43-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39, 40 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants arguments filed on 5/5/2008 have been considered but are not found persuasive.

2. Claims 1-38,41 and 43-75 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/27/2006.

3. Claims 39, 40 and 42 are examined in the instant application.

Declaration under 37 CFR 1.132

The declaration under 37 CFR 1.132 filed 5/5/2008 is insufficient to overcome the rejection of claims 39, 40 and 42 based upon the enablement rejection of record as set forth in the last Office action because the declaration has not been considered. The declaration appears to be an annotated draft. A copy with handwritten changes initialed and dated or a new clean copy would be acceptable.

Information Disclosure Statement

The information disclosure statement filed 5/5/2008 fails to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates

that the list is an information disclosure statement. The information disclosure statement has been placed in the application file, but the information referred to therein has not been considered. The submitted IDS is not in a format that the Examiner can sign and initial each individual format. See PTO form 1449 for reference.

Claim Objections

Claim 39 is objected to because of the following informalities: In line 4 it appears that Applicant, in their amendment, struck through too much language. The word "of" preceding "a subject" is struck out and should be included in the claimed method.

The pending claims encompass non-elected subject matter. The elected subject matter encompasses an SP-C therapeutic that comprises a protein. Applicant should amend the claims to read on the elected invention. The claims are examined only as they relate to the elected invention which comprises a method of treatment comprising the administration of an SP-C protein. Claims 1-38, 41 and 43-75 have the wrong status identifier and should be listed as "withdrawn" and not "original". Applicants in their arguments filed on 1/11/2007 on page 1 state that claims 1-38, 41 and 43-75 are withdrawn from consideration.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39, 40 and 42 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record in the office actions mailed on 4/11/2007, 7/14/2006 and 11/5/2007.

Response to Arguments

Applicants argue in amendment filed on 5/5/2008 that the proteins of the current invention are not systemically acting drugs, which would require transport across cell membranes in non-degraded form in order to maintain activity but rather the present invention work by providing the subject proteins to the mucous layer on the inner surfaces of the lung. Applicants continue to argue that various *in vivo* studies using similar treatments with protein formulations of SP-B and SP-D show that delivery of the protein to the surfaces of the interior of the lung is fully enabled. Applicants continue that surfactant proteins (SP-D, SP-C, and SP-B) have been delivered intra-tracheally in mice; sheep and rabbits, sometimes mixed with carrier lipids to enhance spreading and delivery throughout the lung. Applicants continue that mixtures of SP-B and SP-C in lipid extracts of cow/pig lungs or surfactant isolated from lungs are routinely given for treatment of respiratory distress syndrome affecting pre-term infants, demonstrating that this is a standard therapy for delivery to target surfaces of the lung. Applicants continue that the SP-C surfactant has been shown to be deliverable *in vivo* using known formulations of protein or protein and lipid combinations and that such delivery is able to

deliver a therapeutically effective formulation. Applicants continue to argue that the information in the specification combined with the knowledge in the art demonstrates that one skilled in the art would expect the present invention to work in any respiratory disease involving an inflammatory response due to the similar pathology and etiology show in usage of known therapies with SP-D and SP-B for acute diseases as tested in mice or sheep. Applicants continue that SP-C surfactant has been shown to reduce lung inflammation in a nonspecific, generalized fashion that works regardless of the underlying cause of inflammation. These arguments are not persuasive.

While Applicants have argued that various related surfactant proteins have been delivered *in vivo* to elicit an anti-inflammatory response in the lung, the breadth of the claimed method in view of the teachings in the specification and the art of record still has significant issues regarding enablement of said method. Specifically, claim 39 still encompasses any SP-C therapeutic. While dependent claim 40 defines the therapeutic as a protein, claim 39 recites that "a formulation comprising a SP-C therapeutic" is delivered to a subject. While the elected invention is drawn to an SP-C therapeutic that is a protein, the claimed method still encompasses any SP-C therapeutic, which includes DNA, siRNA, mtDNA, RNAi, small molecules etc. It is noted again that the specification is silent with regard to any guidance to be provided to the skilled artisan as to enable the treatment of airway hyperresponsiveness and/or airflow limitation associated with respiratory disease involving an inflammatory response. The specification rather is drawn to the generation and characterization of SP-C transgenic mice, which comprise targeted disruptions in the SP-C gene thus interfering with SP-C production and designed to mimic SP-C deficiency. Applicants in their arguments have relied upon the use of other

surfactant proteins in the SP family to provide support for the claimed method of treatment. However none of these arguments or references have addressed how delivering an SP-C protein will treat airway hyperresponsiveness and/or airflow limitation associated with a respiratory disease involving an *inflammatory* response. Applicant's argument is that SP-C modifies inflammation, however what does this modification of inflammation encompass? The term "modification" is broad and encompasses decreases/increases in inflammation. It would appear from a reading of the specification that the intended action for SP-C would be to reduce the inflammatory response in the lung. Furthermore, Applicants arguments have failed to teach or show where in the instant specification it is demonstrated that hyperresponsiveness and/or airflow limitation associated with a respiratory disease involving an inflammatory response is actually treated by delivering an SP-C protein. This is significant because Applicants arguments have relied upon SP-C *in vitro* data as well as related SP protein surfactants delivered *in vivo* to substantiate that the claimed method of treatment is enabled. Neither the claimed method nor the specification make any mention that inflammation will be reduced by delivering an SP-C protein to a subject and further that this will treat airway hyperresponsiveness and/or airflow limitation. The skilled artisan has provided no teaching that would link the delivery of an SP-C protein, its effect on any inflammatory response in the lungs of a subject, and a resulting treatment of airway hyperresponsiveness and/or airflow limitation. The claimed method of treatment is not enabled because the skilled artisan cannot reasonably expect, in view of the specification and the teachings in the art, that administering a SP-C therapeutic (protein) will treat airway hyperresponsiveness and/or airflow limitation associated with a respiratory disease involving an inflammatory response. No linkage with inflammation is recited in the claimed method that

would lead the skilled artisan to reasonably expect a change in inflammation that would then ultimately affect airway hyperresponsiveness and/or airflow limitation. The term "associated" is problematic with respect to the claimed method because the skilled artisan cannot determine what is the cause of airway hyperresponsiveness and/or airflow limitation which could be inflammation or another cause such as emphezema. If, as Applicants argue, inflammation is pivotal to the enablement of the claimed method of treatment, the skilled artisan would require teaching demonstrating that delivering an SP-C protein will reduce lung inflammation in a subject and further this reduction in lung inflammation is intrinsically related to airway hyperresponsiveness and/or airflow limitation and not just a mere association. What is not clear to the skilled artisan is whether airway hyperresponsiveness and/or airflow limitation is related to the respiratory disease or the inflammatory response, since again its an association. If airway hyperresponsiveness and/or airflow limitation is the result of the respiratory disease and not just an inflammatory response then the skilled artisan could not reasonably expect that by delivering an SP-C protein that airway hyperresponsiveness and/or airflow limitation will be treated. Thus for the reasons above and of record the rejection is maintained.

No claims are allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DAVID MONTANARI whose telephone number is (571)272-3108. The examiner can normally be reached on M-Tr 8-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 1-571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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